

REMARKS

In item number 3 on page 2 of the Office Action, claims 25-34 were rejected under the judicially-created doctrine of obviousness-type double patenting over the claims of U.S. Pat. No. 5,182,208.

The rejection is traversed for the following reasons.

Throughout the prosecution in the predecessor applications from which benefit is claimed for the instant application, including the first-filed application in the family, claims directed to a method of making a yeast with enhanced astaxanthin content and to a yeast with enhanced astaxanthin content were presented.

All of the Restriction Requirements in the family separated the method of making claims from yeast claims.

Attached hereto are copies of pending claims 1-27. Pages I0724-I0726 depict claims 1-19 as filed, with process of making claims 1-9 and 18-19, and yeast product claims 10-13. Claims 20-27 were introduced by Preliminary Amendment, pages I0997-I1005, and include additional method of making claims 21-27.

Also attached hereto is a copy of the Restriction Requirement for U.S. Serial No. 07/399,183 which matured into U.S. Patent No. 5,182,208, the patent on which the rejection is based, pages I1030-I1043. There it can be seen on page I1031 that the method of making claims 1-9 and 21-27 were restricted from yeast claims 10-13.

Finally, attached hereto is a copy of the Reply to the Restriction Requirement pages I1044-I1046, wherein method of making claims 1-9 and 21-27 were elected without traverse.

The pending claims derive for original claims 10-13 and relate to yeast. Those claims were restricted pursuant to 35 U.S.C. 121 and thus are immune from an obviousness-type double-patenting over a family member application or patent containing claims of another group of claims identified in the Restriction Requirement.

The instant claims are yeast claims, were divided in response to a Restriction Requirement and, accordingly, are subject to 35 U.S.C. 121.

Hence, the obviousness-type double patenting rejection is improper and must be withdrawn.

CONCLUSION

The claims are in condition for allowance and early indication thereof is requested respectfully.

Respectfully submitted,

BELL BOYD & LLOYD LLC

BY 

Dean H. Nakamura
Reg. No. 33,981
Customer No. 29180

Dated: 12 April 2006

We claim:

1. A process for the production of a yeast having an enhanced astaxanthin content, comprising culturing in a nutrient medium containing an antibiotic, cytochrome B inhibitor, or a terpenoid synthetic pathway inhibitor a microorganism of genus Phaffia.
2. A process as set forth in claim 1, wherein the antibiotic is selected from the group consisting of antimycin, tunicamycin, and nystatin.
3. A process as set forth in claim 1, wherein said cytochrome B inhibitor is selected from the group consisting of antimycin and 2-n-heptyl-4-hydroxy-quinoline-N-oxide.
4. A process as in claim 1, wherein the terpenoid synthetic pathway inhibitor is mevalonic acid lactone.
5. A process as set forth in claim 1, wherein the antibiotic or terpenoid synthetic pathway inhibitor concentration in the medium is between 1 and 100 μ M.
6. A process as in claim 1, wherein the antibiotic or terpenoid synthetic pathway inhibitor concentration in the medium is between 30 and 80 μ M.
7. A process as in claim 1, wherein the microorganism of genus Phaffia is subject to mutagenesis either before, after, or before and after morphological selection.

8. A process as in claim 1, employing as said yeast P. rhodozyma ATCC 24230 or ATCC 24202.

9. A process as in claim 1, wherein the astaxanthin in harvested yeast is 1000 ppm or more based on dry weight of yeast cells.

10. A yeast having the identifying characteristics of Phaffia, said yeast having been obtained by at least one step of morphological selection of naturally occurring Phaffia or of a mutant of naturally occurring Phaffia cultured using a medium containing an antibiotic selection agent or a terpenoid synthetic pathway inhibitor.

Phaffia

The mutant yeast of claim 28,

11. A yeast as in claim 10, further characterized by increased sensitivity to antimycin.

Phaffia

The mutant yeast of claim 28,

12. A yeast as in claim 10, further characterized by increased sensitivity to thenoyltrifluoroacetone.

Phaffia

The mutant yeast of claim 28,

13. A yeast as in claim 10, further characterized in lacking the ability to grow on ethanol.

14. A process for increasing the pigmentation of the flesh of salmonids which comprises feeding said salmonids a yeast of claim 10 in disrupted form in sufficient amount to increase the pigmentation of said salmonids.

15. The process of claim 14, wherein said salmonid is salmon.

Sub
C1

ag

ag

ag

16. The process of claim 14 wherein said salmonid is trout.

17. A food supplement comprising the yeast of claim 10 in disrupted form.

18. A process for in vivo production of astaxanthin, comprising culturing one or more times in a nutrient medium containing an antibiotic, a cytochrome B inhibitor, or a terpenoid synthetic pathway inhibitor a microorganism of genus Phaffia, cultivating surviving microorganisms exhibiting enhanced pigmentation, harvesting the cultivated yeast, and extracting the astaxanthin.

19. A process as in claim 17 further comprising subjecting said microorganism of genus Phaffia to at least one mutation either before or after one of said culturings in said nutrient medium containing an antibiotic, cytochrome B inhibitor, or terpenoid synthetic pathway inhibitor.

Sub
C2

add
B3

add
E1

add
E2



PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

7
B
12-6-89

Applicants : ERIC A. JOHNSON, DAVID SCHREIBER, KOWK P. HO,
WILLIAM T. HALL, HUEI-HSIUNG YANG and
BERIL GELDIAY-TUNCER

CIP of
Application No. : 07/229,536 Group Art Unit: 185

Filed : August 8, 1988

For : PROCESSES FOR IN VIVO PRODUCTION OF
ASTAXANTHIN AND PHAFFIA RHODOZYMA YEAST OF
ENHANCED ASTAXANTHIN CONTENT

PRELIMINARY AMENDMENT

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior to consideration on the merits, please amend the
above-identified application as follows:

IN THE SPECIFICATION

Page 15, line 9, after "to" insert - growth in the presence
of a metabolic pathway inhibitor, particularly a main respiratory
pathway inhibitor, in the presence of an influence such as an
agent or environmental condition which triggers a secondary
respiratory pathway, ~~or~~ and

line 10, after "using" insert - a selecting agent, and
particularly--.

Page 32, after the first paragraph, insert

Enhancement of Astaxanthin Biosynthesis

B³ It has also been found that when antimycin or another inhibitor of the main respiratory chain are added to Phaffia rhodozyma cells, and the cells are exposed to light, the astaxanthin content of the yeast is considerably enhanced. The underlying mechanism for this phenomena is not understood, but it could be hypothesized that when the primary respiratory pathway is inhibited, light acts as one of the triggers of a secondary respiratory (oxidative) pathway, having a net effect of considerably stimulating the production of astaxanthin. Thus, the present invention comprises processes for increasing the astaxanthin or other carotenoid content of yeast, comprising growing the yeast in the presence of a metabolic pathway inhibitor while inducing a secondary respiratory pathway. The secondary respiratory pathway may be induced by such influences as light, certain environmental conditions such as those known to cause stress, nutrients, etc. The present invention is, however, not limited by the above hypothesis.

It will be seen from the experiments discussed below that enhanced astaxanthin biosynthesis can be induced by the above mentioned combination of respiratory chain inhibitor with initiation of the secondary respiratory channel.

U.S. APPLICATION NO. 07/229,536
PRELIMINARY AMENDMENT

Example 9

B³ E. rhodozyma strains used were the natural isolate UCD-EST4 67-385 (Phaff et al., 1972; Miller et al., 1976), mutant Ant-1-4 used above, and strain 18-13-6, an astaxanthin enhanced mutant obtained by ethylmethane sulfonate (EMS) mutagenesis procedures (isolated on YM agar). They were grown in yeast extract/malt extract/peptone/glucose medium (YM medium, Difco Co., Detroit, MI) as previously described (An et al., 1989) in a temperature controlled incubator/shaker (Environ-Shaker Model 3597, Lab-Line Instruments, Inc., Melrose Park, IL). Growth was determined by the optical density (660 nm) of a washed cell suspension; 1 mg dry cell weight per ml corresponds to an O.D. of 1.35.

EAT
7/14/88 Light was supplied by two Sylvania 20 watt Coolwhite fluorescent tubes held 20-40 cm from the flask media surfaces. ^{Flasks} Agar media (10 cm diameter) were inoculated with approximately 10^2 - 10^6 cells of actively growing yeast. For dark controls, flasks were wrapped in aluminum foil. When insoluble chemicals were included in the media, they were first dissolved in a small quantity of ethanol (0.3% final conc.), which did not affect yeast growth or pigmentation.

Carotenoid Extraction and Analysis

P. rhodozyma was grown for 5 days in flasks before extraction. Yeasts were harvested from liquid media by centrifugation. The yeast cells were suspended in distilled water, washed in water, and extracted and analyzed for carotenoids by thin-layer chromatography and absorption spectroscopy as previously described (An et al., 1989).

Secondary Respiratory Pathway
Induction Increases Carotenoid Production

The influence of two 20 watt fluorescent bulbs placed 20 cm from the surface of *P. rhodozyma* natural isolate, UCD-FST-67-385, and its antimycin-sensitive mutants, Ant 1-4 and 18-13-6 was studied.

Separate cultures were grown under conditions of (a) total darkness for 30 hours (hereafter "dark"), (b) total darkness with 0.2 μ M antimycin (antimycin being introduced at inoculation) (hereafter "dark/antimycin"), and under conditions (c) and (d) which were identical to (a) and (b) except for exposure of the cultures to light from approximately 30 hours into the experiment until approximately 60 hours into the experiment (hereafter "light" and "light/antimycin").

U.S. APPLICATION NO. 07/229,536
PRELIMINARY AMENDMENT

Extraction of the pigments and characterization indicated that the pigments were qualitatively similar in composition, except that more cis-astaxanthin and lower carotene concentrations were found to be present in light grown cells.

Analysis of yeasts showed that the carotenoid content of light/antimycin P. rhodozyma UCD-FST-67-385 increased by two-fold over any of the dark, dark/antimycin or light cultures of this natural isolate (Table 1). Table 2 shows that mutant 18-13-6, which is antimycin sensitive, produced two-fold increase in carotenoid content in antimycin/light over the light culture.

Table 1

Conditions	Growth (mg/ml)	Carotenoid (µg/g y)
Dark	4.4	520
Dark + Ant	1.6	480
Light	3.3	440
Light + Ant	2.2	1000

U.S. APPLICATION NO. 07/229,536
PRELIMINARY AMENDMENT

Table 2

Antimycin	Not added	Added
Light	Carotenoid Content (μ g carotenoids/g yeast)	
White	540	1410
Blue	1050	1360
Red	960	1210
Dark	830	1013

B³

As can be seen from the above results, growth and carotenoid formation of natural and astaxanthin enhanced E. rhodozyma is clearly influenced by light. The natural isolate, UCD-FST-67-385, and its antimycin-sensitive mutants ant-1-4 and 18-13-6, each grew better and had increased pigmentation in the dark, but were differently affected by light. --

IN THE CLAIMS

Please add the following claims:

-- 20. A process for increasing the pigmentation of the skin, flesh or egg yolk of fowl comprising feeding said fowl a yeast of claim 10 in disrupted form in sufficient amount to increase the pigmentation of said skin, flesh or egg yolk of said fowl.

21. A process for the production of a yeast having an enhanced astaxanthin content comprising subjecting said yeast to growth in the presence of a metabolic pathway inhibitor under an influence which triggers a secondary respiratory (oxidative) pathway.

22. A process as in claim 21, wherein said metabolic pathway inhibitor is a main respiratory pathway inhibitor.

23. A process as in claim 22, wherein the main respiratory pathway inhibitor is present in an amount of from 0.1 to 1.0 μM .

24. A process as in claim 22, wherein the main respiratory pathway inhibitor is glutamic acid.

U.S. APPLICATION NO. 07/229,536
PRELIMINARY AMENDMENT

~~25.9~~ A process as in claim ~~21~~, wherein said influence which triggers a secondary respiratory pathway is light.

B4
B2
25
26. A process for the production of a yeast having an enhanced astaxanthin content comprising subjecting yeast obtained according to claim 1 to growth in the presence of a main respiratory pathway inhibitor and in the presence of an agent or under the influence of an environmental condition which triggers a secondary respiratory (oxidative) pathway.

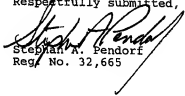
B4
B2
26
27. A process for the production of a yeast of genus P. rhodozyma having an enhanced astaxanthin content comprising inducing an alternative oxidase system by means of growing the yeast in the presence of a main respiratory pathway inhibitor and in the presence of an agent or under the influence of an environmental condition which triggers a secondary respiratory pathway. --

U.S. APPLICATION NO. 07/229,536
PRELIMINARY AMENDMENT

REMARKS

Entry of the above prior to consideration on the merits is respectfully requested.

Respectfully submitted,


Stephan A. Pendorf
Reg. No. 32,665

SUGHRUE, MION, ZINN,
MACPEAK & SEAS
2100 Pennsylvania Ave., N.W.
Washington, D.C. 20037
(202) 293-7060

Dated: August 23, 1989



**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/399,183	08/23/89	JOHNSON	E A54111

SUGHRUE, MION, ZINN,
MAC PEAR & SEAS
2100 PENN. AVE., N.W.
WASHINGTON, DC 20037

EXAMINER
LILLING, H

ART UNIT	PAPER NUMBER
183	12

DATE MAILED: 06/19/91

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

Pat/Elect only

- ☒ This application has been examined ☐ Responsive to communication filed on 5-23-89 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire ONE month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|---|---|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice re Patent Drawing, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152 |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> _____ |

Part II SUMMARY OF ACTION

1. ☒ Claims 1-27 _____ are pending in the application.
Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☐ Claims _____ are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 1-27 _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____ Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 O.D. 11; 453 O.G. 213.
14. ☐ Other _____

Ser No 07/399183
EXAMINER'S ACTION

Serial Number 07/399,183

2

Art Unit 188

15. Receipt is acknowledged of the prior art disclosure statement filed October 7, 1988 in the parent application and amendments filed August 23, 1989.

16. Claims 1-27 are present in the instant application.

17. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-9 and 21-27, drawn to a process for the production of a yeast having an enhanced astaxanthin content, classified in Class 435, subclass 921 .

II. Claims 10-13, drawn to a yeast having the identifying characteristics of Phaffia, classified in Class 435, subclass 255

III. Claims 14-16 and 20 drawn to a process for increasing the pigmentation of the flesh of salmonids or fowl, classified in Class 426, subclass one plus.

IV. Claim 17, drawn to a food supplement comprising the yeast, classified in Class 426, subclass various.

Serial Number 07/399,183

3

Art Unit 188

V. Claims 18-19, drawn to a process for in vivo production of astaxanthin, classified in Class 435, subclass 118.

18. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different products or (2) that the product as claimed can be made by another and materially different process (MPEP 806.05(f)). In the instant case the product claims drawn to the yeast can be obtained from natural sources having the claimed properties.

Inventions II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP 806.05(h)). In the instant case the product can be employed to increase the pigmentation of fowl.

Art Unit 188

Inventions II and IV are related as mutually exclusive species in intermediate-final product relationship. Distinctness is proven for claims in this relationship if the intermediate product is useful other than to make the final product (MPEP section 806.04(b), 3rd paragraph), and the species are patentably distinct (MPEP section 806.04(h)).

In the instant case, the intermediate product is deemed to be useful for obtaining antibiotics and the inventions are deemed patentably distinct since there is nothing on this record to show them to be obvious variants. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 5103 of the other invention.

19. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and divergent subject matter, and because the searches for the individual Groups are not coextensive, restriction for examination purposes as indicated is proper.

20. This application contains claims directed to the following patentably distinct species of the claimed invention:

Serial Number 07/399,183

5

Art Unit 188

i) Whereby the nutrient medium contains:

A. inhibitor

1. cytochrome B
2. terpenoid synthetic pathway

B. antibiotic

- a. antimycin
- b. tunicamycin
- c. nystatin.

ii) Whereby the yeast is

x. P. rhodozyma ATCC 24230

y. P. rhodozyma ATCC 24202.

iii) Whereby the increased astaxanthin is increased in:

q. salmonids

r. fowl

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 8, 10, 18 and 20 are generic.

Serial Number 07/399, 183

6

Art Unit 188

Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a generic claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 of the other invention.

Serial Number 07/399,183

7

Art Unit 188

21. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

Applicant is requested to elect one of the Inventions I-V and to elect a species from i) A or B and/or ii) x or y as appropriate for the elected inventions. Applicant is requested to clearly indicate the claims readable on the elected inventions.

22. Applicant must abide by MPEP 608.01 PC rules pertaining to claiming of biological material. In all patent applications, Applicant must submit a declaration or affidavit meeting the following guidelines:

The declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material.

Serial Number 07/399,183

8

Art Unit 188

- i. Identifies declarant.
- ii. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.
- iii. States that the deposited material has been accorded a specific (recited) accession number.
- iv. States that all restriction on availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.
- v. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the

Art Unit 188

patent application to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 USC 122.

- vi. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer.
- vii. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are

Serial Number 07/399,183

Art Unit 188

10

punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g. see 951 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, name and address of the depository, and the complete taxonomic description.

23. Applicant should note the following decisions which may be pertinent to the claimed language which may be extremely broad for the claimed yeast microorganism.

Serial Number 07/399,183

11

Art Unit 188

A. 217 USPQ 804 Ex parte Jackson

Sufficient information must be given in application so that one of ordinary skill in art can practice invention without necessity for undue experimentation

Description of several newly discovered strains of bacteria having one particularly desirable metabolic property in terms of conventionally measured culture characteristics and number of metabolic and physiological properties does not enable one of ordinary skill in relevant art to independently discover additional strains having same specific, desirable metabolic property, i.e., production of particular antibiotic; in other words, verbal description of new species does not enable one of ordinary skill in relevant art to obtain strains of that species over and above specific strains made available through deposit in recognized depository.

Determination of what constitutes undue experimentation in given case requires application of standard of reasonableness, having due regard for nature of invention and state of art; test is not merely quantitative, since considerable amount of experimentation is permissible if it is merely routine, or if specification in question provides reasonable amount of guidance with respect to direction in which experimentation should proceed to enable determination of how to

practice desired embodiment of invention claimed.

As clearly indicated in Argoudelis 58 CCPA 769, 434 F.2nd 1390, 168 USPQ 99 (1970), the degree of experimentation involved in locating new microorganisms apart from deposited cultures is undue in light of the enablement requirement of 35 U.S.C. 112.

The issue squarely raised by this rejection is whether or not a description of several newly discovered strains of bacteria having one particularly desirable metabolic property in terms of the conventionally measured culture characteristics and a number of metabolic and physiological properties would enable one of ordinary skill in the relevant art to independently discover additional strains having the same specific, desirable metabolic property, i.e., the production of a particular antibiotic.

To state the issue somewhat differently, it is whether a verbal description of a new species would enable one of ordinary skill in the relevant art to obtain strains of that species over and above the specific strains made available through deposit in one of the recognized culture depositories.

The fact that appellants in this case have discovered and deposited three new strains whereas there was only one strain in the Argoudelis case is not seen to materially alter the situation. Discovery of a fourth strain in nature would be

just as non-enabled by the description of the three deposited strains in the present specification as was the discovery in nature of the single strain at issue in Argoudelis.

As clearly indicated in Argoudelis, the degree of experimentation involved in locating new microorganisms apart from the deposited cultures is undue in light of the enablement requirement of 35 U.S.C. 112.

B. 230 USPQ 546 Ex parte Forman et. al.

The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art:....The factors to be considered have been summarized as

the quantity of experimentation necessary,
the amount of direction or guidance presented,
the presence or absence of working examples,
the nature of the invention,
the state of the prior art,
the relative skill of those in that art,
the predictability or unpredictability of the art
and
the breadth of the claims.

Serial Number 07/399,183

14

Art Unit 188

24. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

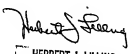
25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Lilling whose telephone number is (703) 308-2034. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

H.J.Lilling: HJL

(703) 308-2034

Art Unit 188

June 18, 1991


HERBERT J. LILLING
PATENT EXAMINER
GROUP 140 - ART UNIT ~~188~~



Handwritten initials

PATENT APPLICATION

*#13.12
B. White
7-5-91*

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : JOHNSON et al.
Application No. : 07/399,183 Group Art Unit: 188
Filed : August 23, 1989 Examiner: Lilling, H.
For : PROCESSES FOR IN VIVO PRODUCTION OF
ASTAXANTHIN AND PHAFFIA RHODOZYMA YEAST
OF ENHANCED ASTAXANTHIN CONTENT

RESPONSE TO RESTRICTION REQUIREMENT

Honorable Commissioner of
Patents & Trademarks
Washington, DC 20031

RECEIVED GROUP 18

JUL 02 1991

Sir:

The following is responsive to the restriction requirement dated June 19, 1991, in the above-identified, for which the Examiner has set a one-month period for response.

In paragraphs 17 and 19 of the restriction requirement, the Examiner requires Applicants to elect one of the specified inventions for prosecution.

Applicants hereby elect invention I, claims 1-9 and 21-27, drawn to a process for the production of a yeast having an enhanced astaxanthin content, without traverse.

Under paragraph 20 of the restriction requirement, the Examiner requires Applicants to elect a single species for prosecution on the merits.

Applicants select:

i) nutrient medium contains:

A. inhibitor

1. cytochrome B

U.S. APPLICATION NO. 07/399,183
RESPONSE TO RESTRICTION REQUIREMENT

- B. antibiotic
 - a. antimycin.
 - ii) the yeast is
 - x. *P. rhodozyma* ATCC 24230.

Under paragraph 22 of the restriction requirement, the Examiner requires Applicants to submit a declaration or affidavit pertaining to depositing of the biological material.

In response, Applicants point out that, under M.P.E.P. §08.01 PC, it is indicated that "no problem exists when the microorganisms used are known and readily available to the public. When the invention depends on the use of a microorganism which is not so known and readily available, Applicants must take additional steps to comply with the requirements of 35 U.S.C. §112."

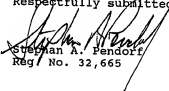
Applicants thus respond to paragraph 22 by urging that the yeast of genus *Phaffia rhodozyma* is known and readily available to the public, as evidenced by the ATCC deposition numbers listed in the specification, thus separate deposition by Applicants is not required.

Under paragraph 23 of the restriction requirement, the Examiner sets forth legal decisions which address patentability of microorganisms.

U.S. APPLICATION NO. 07/399,183
RESPONSE TO RESTRICTION REQUIREMENT

The Examiner has not applied these cases against the present application and they do not appear pertinent. Thus, no response to this paragraph is necessary.

Respectfully submitted,


Sherman A. Pendoff
Reg. No. 32,665

SUGHRUE, MION, ZINN,
MACPEAK & SEAS
2100 Pennsylvania Ave., NW
Washington, DC 20037
(202) 293-7060

Dated: June 28, 1991